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Review

Ethical language and decision-making for prenatally diagnosed lethal malformations

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SUMMARY

In clinical practice, and in the medical literature, severe congenital malformations such as trisomy 18, anencephaly, and renal agenesis are frequently referred to as 'lethal' or as 'incompatible with life'. However, there is no agreement about a definition of lethal malformations, nor which conditions should be included in this category. Review of outcomes for malformations commonly designated 'lethal' reveals that prolonged survival is possible, even if rare. This article analyses the concept of lethal malformations and compares it to the problematic concept of 'futility'. We recommend avoiding the term 'lethal' and suggest that counseling should focus on salient prognostic features instead. For conditions with a high chance of early death or profound impairment in survivors despite treatment, perinatal and neonatal palliative care would be ethical. However, active obstetric and neonatal management, if desired, may also sometimes be appropriate.

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1. Introduction

Antenatal screening, particularly the use of routine mid-trimester ultrasound screening, has altered the diagnosis of major congenital malformations. As a result, in many parts of the world it is now uncommon for major malformations to be discovered at birth [1]. Antenatal diagnosis potentially allows targeted diagnostic testing, planning of delivery, counseling and education of couples, and earlier postnatal intervention for newborns with congenital malformations [2]. However, antenatal diagnosis may identify severe abnormalities where treatment is unavailable, or unlikely to be successful, and where fetal or neonatal death is a likely outcome. Such cases are often referred to as 'lethal malformation' (LM) (Box 1).

The diagnosis of LM is often said to carry ethical and legal implications for management during pregnancy, delivery, and postnatally [3–6]. For example, it may permit obstetric management focused on maternal well-being rather than on fetal survival, termination of pregnancy (including late in pregnancy), or non-resuscitation at birth [7]. But what do we mean when we refer to a malformation as 'lethal'? Which conditions fit into this category? What are the ethical implications of diagnosis of LM?

2. The concept of 'lethal malformation'

The word 'lethal' is derived from the Latin 'letalis' (deadly), and related to a Greek word meaning 'oblivion,' referring to the myth that the souls of the dead forgot their lives on Earth after drinking the waters of the River Lethe. Conventionally, 'lethal' is used to describe something (e.g. an action or agent) that will cause death [8].

In theory, there are several different ways to interpret the description of a malformation as lethal (Box 2).

A review of the published literature on LM revealed no consensus on which of these definitions should be applied [9]. The first definition does not apply to any of the commonly cited LMs, and is not one found in the literature. The second definition is probably the most plausible and the most frequently encountered [5,10–13]. Chervenak and McCullough endorse this definition: 'a lethal condition, properly understood, invariably leads to death, i.e., there is no effective treatment that will prevent a condition, disease, or injury from causing death in the near future' [14]. However, this definition does not apply to any of the malformations that are often described as lethal. Some papers have used the third definition [15–18]. This raises a question about how high a chance of

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Box 1
Malformations most frequently described as 'lethal' conditions [9].

Potter's syndrome/renal agenesis
Anencephaly/acrania
Thanatophoric dwarfism
Trisomy 13 or 18
Holoprosencephaly

death is sufficient to fit into a lethal category. The cited proportion ranges from 50% to 'almost all' [16,19]. There is neither agreement about the correct proportion, nor any obvious way to determine where the cut-off should lie. The fourth definition is used in some epidemiologic studies of neonatal mortality [20–22]. However, it appears far too broad to correspond to the way that LM is used by obstetricians and neonatologists.

3. Which malformations are lethal?

Although Box 1 lists the most frequently cited LMs, more than 25 conditions are included in different lists [9]. No condition was present on all lists, and there was considerable variation.

What is the outcome for these malformations? Table 1 presents an attempt to estimate outcome; however, the values cited are necessarily imprecise. High proportions of affected pregnancies are terminated [47]. Since these conditions are associated with high fetal death rate, survival rate also varies with the gestational age at the time of diagnosis. Postnatal survival is also difficult to estimate because of selection bias in published cohorts, and because of the problem of self-fulfilling prophecies [48,49]. Where a large proportion of infants receive palliative care after birth, a high mortality rate is inevitable [9].

What is clear from Table 1 is that survival of at least six months has been described in all of the conditions frequently cited as lethal. Most strikingly, this includes both anencephaly and bilateral renal agenesis. There has been a very recently published case report of an infant in the USA with Potter syndrome who was treated with antenatal amnio-infusion and neonatal renal dialysis and who survived to be listed for renal transplantation at one year of age.

Box 2
Possible definitions of a 'lethal congenital malformation'.

1. Fetal death: a condition that invariably leads to death in-utero
2. Fetal death/neonatal death: a condition that invariably leads to death either in utero or in the newborn period regardless of treatment
3. Usual fetal/neonatal death: a condition that leads to death in utero or in the newborn period in most cases
4. Associated with death: a condition that leads to fetal or neonatal death in some cases

4. The significance of a 'lethal diagnosis': the examples of trisomy 18 and 13

The severe autosomal trisomies, 18 (Edwards syndrome; T18) and 13 (Patau syndrome; T13), are frequently described as lethal [18,50–53]. Yet, recent population cohort studies show that more than half of affected live-born infants survive for more than a week, and up to 20% survive for more than a year [18,29]. In a large US series including 52,262 very low birth weight infants, 11% of infants with T13 and 9% of infants with T18 survived to discharge [54]. It is possible that even these values represent an underestimate of potential survival rates, since in parts of the world where cardiac surgery is offered to infants with T13 or T18, one-year survival rates as high as 50% have been reported [55].

Why does it matter if these conditions are described as lethal? The first reason to be concerned about this terminology is its potential for misunderstanding and miscommunication. We surveyed more than 1000 obstetricians from the UK, Australia, and New Zealand about the perinatal management of T18 [56]. The overwhelming majority (85%) of obstetricians regarded T18 as a lethal malformation. More than 50% regarded T18 as 'incompatible with life'. We did not ask obstetricians whether they would use these terms in counseling, but a survey of parents from T13/T18 support groups found that 93% had been told by health professionals that their child's condition was 'lethal or incompatible with life' [57]. This contrasts with the evidence summarized above, and with obstetricians' own understanding about survival. Three-quarters of respondents estimated that at least 5% of affected infants would survive for more than one year if treatment were provided [56].

Qualitative studies and narratives from parents of infants with T13 or T18 describe feelings of anger and disillusionment and a sense of being misled by health professionals as well as by the language used [58–61]. Many parents reported that health care providers were unable to look beyond adverse statistics [57]. Furthermore, the Internet has provided families with the ability to do their own research and encounter alternate perspectives on their child's condition. Within seconds of searching for 'trisomy 18' a parent may see pictures of many older children with trisomy 18, smiling and happy, strong evidence against 'incompatibility with life'. If they have been told by their doctor that trisomy 18 is always lethal, there may be repercussions for the family's ongoing capacity to trust health professionals [44].

Another reason to be concerned about denoting a condition such as T18 as 'lethal' is because of a worry that this language contains concealed value judgments about the quality of life of surviving infants [31,49]. Eighty percent of obstetricians in our survey believed that T18 was not compatible with a 'meaningful life' [56]. Labeling a condition as 'lethal' may also risk taking decision-making from the parents [31,49]. In our survey, 23% of obstetricians would never discuss or offer fetal monitoring in labour for women after an antenatal diagnosis of T18, and 28% would never offer caesarean section for fetal distress [56]. In the parent-support group study, two-thirds of parents reported feeling pressure to terminate their pregnancy [57].

There is a concept in medical ethics that shares some features with that of LM: the concept of 'medical futility' [9,19]. Medical futility emerged in the 1990s as a potential way to resolve disputes between patients and doctors about life-sustaining treatment [62]. It reflected a perceived need by medical professionals to limit patient autonomy and to justify a decision not to provide treatment that had been requested [62]. The basic idea was that although it was important to respect patients' views about treatment, health professionals were not obligated to provide futile treatment [63]. However, the concept of futility has fallen out of favour because of a

Table 1
Published outcome for severe congenital anomalies often described as lethal.[a]

Severe congenital anomalies	Prevalence	Probability of live birth (in absence of termination)	Median postnatal survival	Proportion surviving >1 week/>1 year	Longest reported survivals
Renal agenesis	1.7/10,000 [23]	Not reported	<24 h [23]	<5%	13 months [97,98]
Anencephaly	10/10,000 pregnancies 2.6/10,000 births [24]	62–72% [25,26]	<24 h [26,27] 55 min [28]	0–14%>1 week/7% >1 year [18,29]	10 months [30] 2.5 years [31]
Thanatophoric dysplasia	0.4/10,000 [32]	Not reported	Not reported	Not reported	5 years [33] 9 years [34]
Trisomy 18	2.6/10,000 [24]	48–51% [35,36]	14 days [37]	35–65%>1 week/14–19% >1 year [18,29]	27 years [38] 30 years [39] 50 years [40]
Trisomy 13	1.2/10,000 [24]	28–46% [35,36]	10 days [37]	45–57%>1 week/14–21% >1 year [18,29]	19 year [41] 27 year [42]
Holoprosencephaly	0.5/10,000 [43]	Not reported	4–5 months [44]	71%>1 week/ 47% >1 year [29]	6 years [45] 11 years [44] 13 years [43] 19 years [46]

[a] Using recent population cohort studies where available.

number of serious problems in parallel with the concept of LM [64,65].

First, there is a problem with defining futility. There have been at least five different definitions proposed, and no agreement on which should be used [64]. Some authors distinguish quantitative from qualitative futility [63]. Treatment is quantitatively futile if it has a very low chance of success. However, just as for the third definition of LM, there is a problem with determining where the statistical threshold should lie. Is a 90% chance of death high enough, or should it be 95% or 99%? Trisomy 13/18 might appear lethal on some definitions, but not others.

Second, even if a particular statistical threshold is used, there is a problem with determining whether treatment would actually be futile in an individual case. Even if treatment has not succeeded in the past, there may have been technological changes that could potentially improve survival. There may be specific features for an individual patient that distinguish him from aggregated cohorts. (For example, a fetus with T18 might have a structurally normal heart and appear to have better prognosis, or might have hypoplastic left heart and have a much worse prognosis than average [66].) Often there are limited data on which to base a prognosis. The problem of self-fulfilling prophecies means that available data may not be representative of actual chances of survival if treatment were provided [48].

Third, the clearest and strictest available definition appears to exclude almost all actual cases. Treatment is said to be 'physiologically futile' if there is no way for it to achieve its physiologic aim [62]. For example, cardio-pulmonary resuscitation would be physiologically futile if there were literally no ability for it to restore circulation and breathing. Analogously, a condition might be denoted lethal (using the second definition) if survival is impossible regardless of treatment. However, either of these definitions appears to render the concept relevant only in extremely rare cases, and certainly not in T13 or T18.

Fourth, there is a concern that the term 'futile', particularly when it is used qualitatively, amounts to 'giving opinion disguised as data' [67]. Treatments are described as being 'qualitatively futile' when treatment might be able to sustain life but is not perceived to amount to a benefit for the patient. For example, providing intensive care to a patient in a persistent vegetative state has been described as being qualitatively futile [63]. Similarly, some definitions of LM include conditions associated with a persistent vegetative state or absent cognitive development [6,10,68,69]. In our survey of obstetricians, 20% indicated that the best developmental outcome in T18 is a vegetative state [56]. Yet, available data suggest that children with T18 and T13, although usually profoundly impaired, are not vegetative. Surviving children are reported to be aware of those around them, to hear and respond to sound, and to learn and remember [39]. Most are unable to speak, yet are able to communicate non-verbally at a basic level [70]. Whether this level of function is sufficient to outweigh the burdens of treatment constitutes an important ethical question. It may or may not be in the best interests of a child to provide particular treatment given this prognosis [52,68,71]. However, it is clear that this involves a judgment about the value of life in a severely impaired cognitive state. Professional guidelines strongly endorse the idea that counseling following prenatal diagnosis should be non-directive and value neutral [72–74]. Whereas some authors have questioned whether complete neutrality in counseling is possible or desirable [72,75–77], there are good reasons for doctors to aspire to neutrality in most circumstances. One important way to do this is to avoid language that contains implicit value judgments [78].

5. Beyond the concept of 'lethal malformations'

We have criticized the concept of LM, but what does that mean for counseling or for decision-making?

It might be possible to find an alternative term to describe all of the congenital conditions that are usually referred to as lethal. They appear to share a high chance of death and profound impairment regardless of attempted treatment. We could refer to 'life-limiting' conditions [79], 'poor prognosis' malformations, or 'potentially lethal' [79] malformations. However, any new term will have the same problems of defining the probability and severity of poor outcome that would justify its application. Unless it is a term that parents easily and reliably understand, it will need to be explained. Instead, we have previously suggested that it would be better for counseling to openly and honestly address the key prognostic questions that parents are likely to ask after diagnosis of a severe congenital malformation [9].

1. Diagnosis: what is the diagnosis, and how certain can practitioners be?
2. Neonatal survival: what is the chance of survival past the newborn period if treatments (including intensive life-prolonging therapies) are provided?
3. Long-term survival: how long is the child likely to survive if life-sustaining treatment is provided?
4. Long-term impairment and illness: if the newborn survives, what long-term health problems and impairments are they likely to experience? What is the range of possible outcomes?
5. Burden of treatment: what treatments would be required to keep the newborn infant alive, and how burdensome would these be for the child and the family?

The most important ethical question is what treatment should be offered or provided to women and to fetuses and babies in the setting of severe congenital malformations with a very high chance of death or profound disability despite treatment. We have argued that such malformations should not be called 'lethal'. However, the label should not change the treatment that is provided. The label that we give to conditions is not ethically relevant to the options that are appropriate. One additional advantage of avoiding the 'lethal' designation may be that these conditions are not identical. If we treat each condition (and indeed each child) on its merits, options may be appropriate in some circumstances and not in others.

Which options, then, should be provided to severe malformations such as those in Box 1? For all, the option of palliative care at birth should be given to parents. The high chance of death or profound impairment means that it is questionable whether providing resuscitation and life-prolonging treatment is in the child's best interests [80]. It is critical that high quality palliative care is available to the infant and family [4,81]. It is important, though, to ensure that parents and future parents are aware about variable duration of survival. Provision of palliative care does not necessarily mean that the child will die quickly [82]. Palliative support does not need to be confined to the postnatal period, and there may be considerable benefit to the family by offering a palliative approach from the time of diagnosis, through to delivery, and beyond [3,83,84]. There are perinatal palliative care programs available in an increasing number of centres. A palliative (maternal-focused) approach to obstetric care may mean that it is appropriate to avoid monitoring in labour and to aim for vaginal delivery, if that is consistent with a woman's wishes [6,85–87].

If palliative care is an option, what about the opposite? Should resuscitation and intensive care be an option? Should fetal-oriented obstetric management be available? Here a nuanced answer is needed that takes into account the specifics of each case. Nevertheless, we support the recommendation that an active approach to obstetric management, including fetal monitoring, cesarean section, and resuscitation, may be appropriate even in the face of a high death rate [14,85,88,89]. Such treatment is not contrary to the interests of the child [89]. For some parents, the opportunity to experience some time with their child while s/he is still alive may be extremely important [88]. On the other hand, this does not mean that unlimited treatment should be made available if requested by parents [90]. Invasive and intensive treatment, particularly if prolonged, may not be in the interests of the child in the face of very low chance of benefit. Such treatment may also be unreasonable in the setting of limited public health resources [62]. Health professionals may be justified in declining treatment in such circumstances. However, such decisions must be made on the basis of the child's specific circumstances, and on consistently and transparently applied ethical principles rather than on the basis of a label of 'lethality'.

What about termination of pregnancy? The diagnosis of LM would make no difference to decisions about termination in jurisdictions that either do not permit termination on fetal grounds, or alternatively that allow access to termination for a broad range of fetal abnormalities. However, in some jurisdictions the diagnosis of a 'lethal' malformation may permit termination of pregnancy, even at a gestational age when this would otherwise be prohibited [91]. For example, the Texas Health and Safety Code [92] makes an exception to the prohibition of pregnancy termination after 20 weeks if 'the fetus has a severe and irreversible abnormality', defined as 'a life threatening physical condition that … regardless of the provision of life saving medical treatment, is incompatible with life outside the womb' [93]. Similarly, the Columbian Penal Code permits termination "when there are serious malformations of the fetus that make the fetus not viable, as certified by a medical doctor' [94]. The terms 'not viable' and 'incompatible with life' appear to relate to LM, and might have been intended to refer to conditions listed in Box 1. Yet, the analysis indicates that anencephaly and even bilateral renal agenesis are potentially compatible with long-term survival and are 'viable' on strict definitions. If so, women carrying fetuses with LM may be unable to access termination.

It is beyond the scope of this paper to provide a detailed discussion of the legal or ethical approach to abortion law. Nevertheless, it is not our intention to limit women's options. For jurisdictions that regard LM as a special case and wish to allow abortion in such cases, there are perhaps three possibilities. One possibility would be for lawmakers to create specific exceptions for conditions such as those listed above. For example, the Brazilian Supreme Court ruled that termination is permissible after diagnosis of anencephaly (though not in other situations) [95]. Other conditions could be added to this list, although in practice there may be significant hurdles in achieving such a law change. A second possibility would be to leave it to medical professionals to decide which conditions are sufficiently severe to be regarded in law as 'lethal' or non-viable. The Columbian constitutional court has ruled that 'determinations are to be made by medical practitioners acting within the ethical standards of their profession' [94]. However, the lack of medical consensus about which conditions can and should be considered 'lethal' would potentially lead to inconsistent determinations and decision-making [85,96]. A third possibility would be to draft legislation that sets out the specific ethical preconditions for permitting termination of pregnancy. For example, Chervenak and McCullough have argued that termination of pregnancy should be permitted in the third trimester for conditions with a high degree of certainty of diagnosis, and 'a very high probability of either death or survival with severe and irreversible deficit of cognitive developmental capacity' [7,14]. This would appear to include all of the conditions in Box 1.

6. Conclusions

In this review, we have analysed and criticized the concept of 'lethal' congenital malformations. The term is misleading, and potentially leads to miscommunication with families and inconsistent decision-making. None of the malformations frequently described as 'lethal' fits with strict definitions of this term. However, even if they are not lethal, the severity of conditions such as anencephaly, renal agenesis, and T13/T18 means that perinatal palliative care, maternal-focused obstetric care, and potentially termination of pregnancy are justified. It may also be appropriate to provide fetal-oriented obstetric care and some life-sustaining treatments for these conditions where this is consistent with a woman's wishes and the child's best interests.

Practice points

- Survival beyond the newborn period has been described in all of the congenital malformations that are often described as being 'lethal'.
- The terms 'lethal malformation' or 'incompatible with life' should be avoided in counseling.
- A palliative approach to management during pregnancy, delivery, and postnatally may be ethically appropriate for fetuses with a very poor prognosis.
- An active approach to obstetric and neonatal care may also be appropriate in these conditions to enable parents to experience some time with their child while alive.

Research directions

- Research is needed on parental response to language and counseling approaches following diagnosis of severe congenital malformations.
- There are few data on how frequently parents would choose active or palliative approaches to care following diagnosis of severe congenital malformations.
- There is a need to evaluate the impact of antenatal and postnatal decisions on parents' long-term well-being.

Conflict of interest statement

None declared.

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